The HBsAg-Positive Patient

Implications and a Guide to Management

R. P. BRYCE LARKE

SUMMARY

Following infection with hepatitis B virus (HBV), hepatitis B surface antigen (HBsAg) is detectable in the serum before liver function tests become abnormal and before development of clinical features of hepatitis; HBsAg tests usually become negative shortly after illness subsides. Screening individuals such as volunteer blood donors for HBsAg occasionally reveals apparently healthy people who are persistent carriers of HBsAg; the majority have no laboratory evidence of hepatitis whereas others have biochemical or histologic findings of chronic liver disease. (Can Fam Physician 25:317-319, 1979).

Dr. Larke is professor of pediatrics and honorary professor of medicine, Division of Infectious Diseases, as well as clinical virologist at the Provincial Laboratory of Public Health, University of Alberta. Reprint requests to: Provincial Laboratory of Public Health, The University of Alberta, Edmonton, AB. T6G 2J2.

DURING THE PAST DECADE, increasing numbers of physicians have been receiving reports indicating that a patient is positive for hepatitis B surface antigen (HBsAg), formerly known as Australia antigen. Sensitive laboratory tests for HBsAg, the practical results of Blumberg's Nobel prize winning observations which began in 1963,[1] are now readily available to most physicians throughout Canada. In many instances, the physician has ordered HBsAg testing as part of the laboratory investigation of a patient with jaundice, hepatomegaly or other evidence suggesting acute or chronic liver disease. However, in other instances, the laboratory test has not actually been requested by the physician himself: the usual situation is that volunteer blood donors are routinely screened serologically for HBsAg. This practice has effectively reduced the incidence of post-transfusion hepatitis B virus (HBV) infection, since blood from all HBsAg-positive donors is rejected. In some localities, sera submitted to the Red Cross for Rh antibody determinations during pregnancy have also been screened for HBsAg.

HBsAg is a component of the outer protein coat of the 'Dane particle' (considered to be the complete hepatitis B virus) which appears in the blood in relatively large quantities during an infection known previously as serum hepatitis.[2] A variety of laboratory tests may be used to detect HBsAg, including direct electron microscopic examination of serum. Serologic assays make use of specific antigen-antibody interactions, the most widely used at present being a very sensitive solid-phase radioimmunoassay (RIA).

Significance of a Positive Test

A person who is HBsAg-positive may be:

1. in the incubation phase of HBV infection.
2. undergoing acute icteric or anicteric hepatitis B.
3. recovering from icteric or anicteric hepatitis B.
4. an asymptomatic carrier of the antigen.
5. suffering from chronic liver disease.

Feinman and his colleagues[3] have published a very useful guide to the assessment of patients who are positive for HBsAg, including a table based on the presence of clinical signs and symptoms of hepatitis and the results of liver function tests.

The incubation period of hepatitis B is usually 60-90 days, but may range from 45-160 days or longer. Symptoms, if they develop at all, are usually insidious in onset and may consist of vague abdominal discomfort or a prodromal serum-sickness-type syndrome characterized by skin rash (often urticarial), polyarthralgia and arthritis.[4] HBsAg appears in the serum several weeks before onset of the above clinical features or slowly progressing jaundice; it may approach peak levels by the time liver function tests such as serum glutamic pyruvic transaminase (SGPT) become abnormal. In most patients with acute hepatitis B, HBsAg will become undetectable and transaminase levels will return to normal shortly after the clinical illness subsides. Antibody to HBsAg, known as anti-HBs, usually appears in the serum a few weeks after clearance of HBsAg and persists for many years thereafter.[5,6]

Approximately ten percent of people infected with HBV fail to clear HBsAg from their blood. The immunologic aspects of HBV infection and mechanisms which may be responsible for persisting antigenemia are discussed elsewhere.[7-9] Individuals who are apparently healthy, and who do not recollect having had icteric hepatitis in the past, may be identified as HBsAg-positive only when they volunteer as blood donors. Routine screening by the Canadian Red Cross Blood Transfusion Service indicates that about 0.15% of first-time volunteer donors are positive for HBsAg; these people are advised to contact their physician for further investigation.

The first step in following up people found to be HBsAg-positive is to repeat the serologic test and ensure that the assay is specific rather than a false-positive reaction. Even if the person feels completely well and has no abnormal physical findings, he or she may nevertheless be in the incubation

period or early prodromal phase of acute hepatitis B or may be recovering from a subclinical infection; under these circumstances, liver function tests such as the SGPT may be abnormal. Re-examination within the next one or two weeks should reveal a persistently positive assay for HBsAg, abnormal liver function and perhaps the development of physical signs or symptoms of hepatitis if the initial HBsAg testing had taken place in the early stages of HBV infection.

Patient follow-up should continue for at least four months after the initial report of a positive HBsAg assay. If clinical findings and liver function tests remain normal despite persistence of HBsAg, the patient is considered to be an asymptomatic carrier of the antigen and liver biopsy is not indicated. However, if liver function tests are consistently abnormal, the liver should be biopsied. There is usually histologic evidence of chronic benign hepatitis. The patient can be reassured that the condition is not progressive but yearly assessment for liver disease is recommended. Occasionally the liver biopsy may unexpectedly show evidence of chronic active hepatitis, compensated cirrhosis or other forms of chronic liver disease.[3]

The HBsAg Carrier

As outlined above, an individual who remains HBsAg-positive for more than four months is considered to be a carrier of the antigen. There is a predisposition to development of the HBsAg carrier state among patients on longterm hemodialysis, those with underlying malignancy or on immunosuppressive therapy and longterm residents of large facilities for the mentally handicapped. Other factors which influence the proportion of HBsAg carriers in a given population include geographic location, ethnic origin, socioeconomic conditions as well as the incidence of drug abuse and male homosexuality.[3, 10] The majority of asymptomatic carriers found on routine screening of blood donors for HBsAg have no clinical, biochemical or histologic evidence of liver disease and may be defined as healthy carriers.[3, 11]

Considerable attention has been given to HBsAg carriers' potential for transmitting HBV infection to their contacts.[11] This problem is of particular concern amongst health care workers who may be exposed, often unwittingly, to people who are HBsAg-positive. Hospital personnel exposed to hemodialysis or renal transplant patients, or staff employed in clinical laboratories, are at increased risk of acquiring HBV infection.[12, 13] Personnel associated with operative and anesthetic procedures and nurses caring for patients with hepatitis are positive for HBsAg and anti-HBs more frequently than other hospital workers.[14, 15] Detection of anti-HBs in the serum indicates past infection with HBV, either clinical or subclinical, and the test for antibody has proven useful in epidemiologic studies to determine patterns of transmitting infection.

Recent studies have shown that, in Canada, dentists are not at increased risk of acquiring clinical hepatitis or becoming HBsAg carriers, even though there is evidence of increased exposure to HBV infection, indicated by the proportion of dentists positive for anti-HBs.[16] A report from another country where the HBsAg carrier state and hepatitis B are prevalent indicated that routine dental care was not an important factor in the spread of HBV infection.[17]

Concern has also been raised that HBsAg-positive health care personnel may represent a source of infection for other hospital patients and staff. A review of the available epidemiologic data indicates that HBV transmission does occur but seems to be very rare.[18] Minute amounts of blood or serum transferred during routine hospital procedures seem to be the cause of infection. Minor lesions on the hands are probably the source of infective blood which is then introduced into contacts by oral or percutaneous routes.

There has recently been considerable interest in another antigenic determinant associated with HBV—the 'e' antigen (HBeAg) and its corresponding antibody, anti-HBe. There is a correlation between the presence of HBeAg and the relative infectivity of HBsAg carriers.[2, 19-21] At present, tests for HBeAg and anti-HBe are carried out at only a few reference laboratories and research centres in Canada and are therefore not routinely available to physicians. This situation may change within the very near future when an RIA for HBeAg becomes marketed commercially. However, the usefulness of testing HBsAg carriers for HBeAg as a guide to contagiousness is not yet clear.[22] Until more is known about the value of HBeAg or other serologic markers which may be indicators of infectivity, such as antibody to hepatitis B core antigen (anti-HBc) and DNA polymerase,[2] and until these tests become widely available, anyone positive for HBsAg should be considered capable of transmitting hepatitis B.

What should be done with the identified carrier of HBsAg? Some judicious guidelines to deal with this difficult problem have been suggested.[11, 22] HBsAg carriers should be excluded as blood donors. They should be offered a clinical examination and laboratory screening for liver diseases and provided with whatever medical follow-up may be warranted on clinical grounds. Although hepatitis B may be transmitted among household contacts of HBsAg carriers over a period of years, overt liver disease is uncommon and the physician should avoid advice that may make the carrier seem to be a health hazard. Screening of family contacts for possible immunity to hepatitis B may provide reassurance if the anti-HBs test is positive, but may only increase anxiety if negative. Mosley[22] has wisely pointed out the importance of exercising judgment based on the emotional climate in the family involved.

The HBsAg carrier should be advised about potential means of transmitting hepatitis B through exposure to infective blood, plasma or saliva. Personal items such as razors and toothbrushes should not be shared, sanitary pads or tampons should be disposed of carefully and special attention paid to thorough handwashing.

Practical Problems

A number of problems requiring a decision about HBV infection arise when a HBsAg-positive patient becomes pregnant.

1. *Clinical status of the pregnant patient*

The patient may have been identified as HBsAg-positive as a result of some routine screening procedure or during investigation for possible viral hepatitis. Differentiation between acute or chronic liver disease, transient or persistent antigenemia and identification of the patient who is a healthy HBsAg carrier have been discussed above.

2. *Risks to the child*

Acute hepatitis B in the mother has been associated with an increased inci-

dence of premature delivery (at or before 37 weeks gestation), particularly if the onset of maternal hepatitis is in the third trimester.[23, 24]

Approximately two-thirds of women who develop acute hepatitis B during the third trimester of pregnancy or within two months following parturition will transmit HBV to their infant. The risk of transmission is probably less than ten percent if acute hepatitis develops earlier in pregnancy or if the mother is a chronic asymptomatic carrier of HBsAg. Most infants remain clinically healthy despite development of chronic, subclinical hepatitis and persistence of HBsAg in their blood.[25] Although the exact mechanism of HBV transmission from the mother remains uncertain, transplacental infection may occur or infants may aspirate or ingest infective blood during delivery. The majority of infected infants do not become HBsAg-positive until after the first month of life.

HBsAg has been detected in breast milk, but there is no evidence that infants have acquired HBV infection by this route and there seems no reason to discourage breastfeeding by otherwise healthy HBsAg carrier mothers who wish to do so.[24, 26, 27]

Although the great majority of perinatally-acquired HBV infections do not appear to have any adverse effects on the child's early growth and development, severe hepatitis occasionally develops and may affect successive infants born to a chronic HBsAg carrier.[28] Consideration should be given to preventing HBV infection by passive immunization of the infant with hepatitis B immune globulin (HBIG) very soon after birth, particularly if there is a family history of previous neonatal hepatitis.[24, 29] HBIG is not currently licensed for use in Canada but it can be obtained for investigational purposes (including those mentioned in this article) by contacting the local branch of the Canadian Red Cross Blood Transfusion Service.

3. *Management of contacts*

Risk of transmission of acute hepatitis B is relatively greater for the sexual partner. This contact should be tested for HBsAg: if negative, consideration should be given to the administration of HBIG or possibly standard immune serum globulin (ISG) which contains some anti-HBs.[30]

If the spouse is positive for anti-HBs, no further action is necessary since such persons are generally considered to be immune to hepatitis B.

4. *Risks to health care personnel*

Some consideration of the risks to health care personnel presented by HBsAg carriers is outlined above. In the case of pregnant women, whether they are asymptomatic HBsAg carriers or have acute hepatitis B, there is potential risk of transmitting infection to personnel in the labor and delivery rooms and to those handling the lochia or other blood-contaminated discharges following parturition. However, it is impractical and unnecessary to impose restrictive isolation on asymptomatic HBsAg carriers in hospital, provided they observe careful handwashing techniques and other general hygienic precautions.

As mentioned above, limited supplies of HBIG are available in Canada through the Red Cross Blood Transfusion Service and a protocol for its use in accidental exposures has been established. If HBIG is unavailable, the administration of standard ISG which contains some anti-HBs may be beneficial.[21, 30]

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